

For the Medical Profession only

'BENZEDRINE'

BRAND

TABLETS



Each tablet contains 5 mg. (0.077 gr.) of
 β -Phenylisopropylamine Sulphate
(Isomyn Sulphate).

'Benzedrine' Brand Tablets stimulate the central nervous system and have a good effect upon depressed mood. They relax smooth muscle of the gastro-intestinal tract, and, in the higher dose ranges, produce a rise in blood-pressure.

The therapeutic application of 'Benzedrine' Brand Tablets is indicated in a number of clinical conditions where the effects mentioned above have been shown to be desirable.

IMPORTANT

It is strongly urged that physicians intending to use 'Benzedrine' Brand Tablets should first read this new circular—especially the section on DOSAGE (p. 7).

' BENZEDRINE '
BRAND
TABLETS

ARE ISSUED IN BOTTLES OF 50.

Each tablet contains 5 mg. (0.077 gr.)
 β -Phenylisopropylamine Sulphate (Isomyn
Sulphate) and is grooved so that it may
easily be broken into halves.

NOTE.—' Benzedrine ' Brand Tablets should not
be confused with the Benzedrine Brand Inhaler.
The tablets are *not* intended for use in head colds,
sinusitis, hay fever, or other common
nasal conditions.



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For Smith, Kline & French Laboratories,
owners of the Registered Trade Mark, ' Benzedrine '



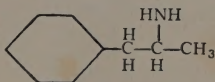
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'BENZEDRINE'

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TABLETS

'Benzedrine,'* β -phenylisopropylamine or isomyn, $C_6H_5 \cdot CH_2 \cdot CH(NH_2)CH_3$, is a sympathomimetic compound structurally related to ephedrine and epinephrine.



CENTRAL NERVOUS SYSTEM STIMULATION

'Benzedrine' has a profoundly stimulating effect upon the central nervous system. The effect is prolonged, lasting from two to several hours.^{1,7,14} This stimulatory action has made the drug of value in the treatment of various neurological conditions.

Using 'Benzedrine' Brand Tablets in narcolepsy, Prinzmetal and Bloomberg² reported complete relief of sleep attacks and almost complete relief of cataplexy when it was present. Their work has been confirmed by other investigators.^{3,11,17} Favourable results in the symptomatic treatment of post-encephalitic Parkinsonism have been reported. In this condition 'Benzedrine' may be used alone, but Solomon, Mitchell, and Prinzmetal found it usually more effective when combined with scopolamine or stramonium.¹⁵

* 'Benzedrine' is the Registered Trade Mark of Smith, Kline & French Laboratories to designate their brand of Isomyn (β -Phenylisopropylamine).

EFFECT ON MOOD

'Benzedrine' has a good effect upon depressed mood if administered in small doses. The effect is not accompanied by any change in personality or any clouding of the mentality. There appears to be no subsequent period of 'let-down' below the previous normal level. Though it probably does not operate against major disturbances such as are seen in mental disease, yet it tends to banish fatigue and depression in the milder depressive neuroses.

Myerson⁷ reported 'Benzedrine' Brand Tablets of value in dispelling morning apathy and depression in certain mild depressive neuroses; Nathanson¹⁴ found a subjective sense of well-being one of the most consistent effects following ingestion of the drug; and Davidoff and Reifstein¹⁸ have published a detailed comparison of its stimulating action on a group of normals and five groups of abnormal patients. Wilbur, MacLean, and Allen¹³ reported improvement in 70 per cent. of a series of patients suffering from simple depressions and the depressions accompanying certain psychoses. Results were less favourable in a group of psychoneurotic patients with symptoms of nervousness, anxiety, and inability to relax.

EFFECT ON MENTAL ACTIVITY

Peoples and Guttman⁴ found that 'Benzedrine' accelerates mental processes and enhances accuracy, and from observations on over 250 patients Guttman and Sargent¹⁷ have described the general psychological stimulation that follows its use. Sargent and Blackburn⁹ reported over 8 per cent. improvement in intelligence scores following the administration of 'Benzedrine,' and Davidoff⁸ found that the mental stimulation due to the drug was helpful in the management of certain types of self-absorbed patients.

CHRONIC FATIGUE

In a group of patients suffering from persistent exhaustion, Nathanson¹⁴ reported marked amelioration of fatigue in 80 per cent., and increased energy and capacity for work in 50 per cent. Wilbur, MacLean, and Allen¹³ reported improvement in 75 per cent. of a group of patients whose chief complaints were fatigue, lack of energy, and lassitude.

GASTRO-INTESTINAL EFFECT

In the higher dose range 'Benzedrine' relaxes smooth muscle of the gastro-intestinal tract and relaxes spasm, whether of functional, reflex, or organic origin. Relaxation usually occurs within a few minutes after administration.^{5,10}

The tablets have been found of value in X-ray visualization of the gastro-intestinal tract after a barium meal. Myerson and Ritvo⁵ obtained more accurate differential diagnosis between functional and organic spasm and also better visualization of lesions.

PRESSOR ACTION

In the higher doses 'Benzedrine' Brand Tablets usually cause an appreciable rise in blood-pressure which may persist for several hours.^{4,6} This pressor effect has been found of value in the treatment of three cases of orthostatic hypotension.^{12,16}

TOXICITY

'Benzedrine' may be considered virtually non-toxic in therapeutic doses. In rats the Minimum Lethal Dose intravenously has been established as approximately 35 mg. per kg.^{1,19} The margin of safety appears to be wide. If one may transfer the data on toxicity in rats to humans on a weight basis, the Minimum Lethal Dose would be approximately seventy to one hundred times as great as the therapeutic dose.

Moreover, animals which survived large, sub-lethal doses over a long period of their normal life-cycle showed no pathologic lesions on post-mortem tissue examination.

Craving or addiction has not been reported; but, as with most drugs which are effective in relieving unpleasant symptoms, such a possibility must always be borne in mind. Because of the untoward reactions which may follow its abuse, 'Benzedrine' Brand Tablets should be administered only to those patients whose activities are closely directed by the physician.

Overdosing is characterized by dilatation of pupils, sleeplessness, and inability to relax. Reduction of dosage is usually sufficient, but, if necessary, these symptoms may be controlled by mild sedatives such as the barbiturates.

CONTRA-INDICATIONS

'Benzedrine' Brand Tablets are contra-indicated where there is great excitability, manic or hypomanic tendencies, and insomnia. *Except in certain special cases, the tablets should not be given in late afternoon or evening. (See DOSAGE.)*

Inasmuch as large doses may have a pressor effect, the drug should be used with caution in hypertensive cases. It should also be remembered that atropine, stramonium, and scopolamine enhance its pressor effect. Although it appears to have no bad effect on the normal heart, 'Benzedrine' should not be used in the presence of coronary disease.

Since 'Benzedrine' Brand Tablets relax pyloric spasm, their use is inadvisable where there is a pre-existing atonicity in the gut. As with atropine, the use of 'Benzedrine' is often followed by a drying of the secretions of the mouth and sometimes by loss of appetite.

The tablets should be discontinued in patients who show, by reactions to initial small doses, that they are hypersensitive to ephedrine-like compounds.

Moreover, it should be borne in mind that undue stimulation through unsupervised and constant use may lead to excessive activity, both mental and physical, uncompensated by sufficient sleep. It is important, therefore, to prevent the patient from abusing the usefulness of 'Benzedrine.'

DOSAGE

Until the precise action of 'Benzedrine' Brand Tablets upon the nervous system is more fully studied, the question of dosage should be approached with caution. The balance between the sympathetic and the parasympathetic nervous systems is a delicate one, varying considerably with the individual. Any sympathomimetic drug, therefore, may have effects which are at present unpredictable, except along broad general lines.

Initial doses should be small—in fatigue and depressive states, 2.5 mg. to 10 mg. Administration in the late afternoon or evening may interfere with sleep.

In narcolepsy the dose range has been from 10 mg. once daily to 30 mg. three times daily.^{2,3,11} In post-encephalitic Parkinsonism the average dose has been 10 or 20 mg. two or three times daily.¹⁵ For X-ray visualization 10 to 30 mg. were given at a time.^{5,10} An initial small test dose may be advisable to eliminate the possibility of individual hypersensitivity. The dose in depression or fatigue states and for mental stimulation has varied from 2.5 mg. to a maximum of 20 mg. once or twice daily, depending upon the individual patient.^{7,8,13,14}

Where divided doses are required, the specially grooved tablets may be broken into halves.

REFERENCES

1. G. A. ALLES: The Comparative Physiological Actions of the dl- β -Phenylisopropylamines. I. Pressor Effect. *Jour. Pharmacol. & Exper. Therap.*, 1933, xlvii, 339.
2. M. PRINZMETAL AND W. BLOOMBERG: The Use of Benzedrine for the Treatment of Narcolepsy. *J.A.M.A.*, 1935, Dec. 21, cv, 2051.
3. H. ULRICH, C. E. TRAPP, AND B. VIGDOFF: The Treatment of Narcolepsy with Benzedrine Sulphate. *Ann. of Int. Med.*, 1936, March, ix, 1213.
4. S. A. PEOPLES AND E. GUTTMANN: Hypertension produced by Benzedrine: Its Psychological Accompaniments. *Lancet*, 1936, May 16, 1107.
5. A. MYERSON AND M. RITVO: Benzedrine Sulfate and its Value in Spasm of the Gastro-intestinal Tract. *J.A.M.A.*, 1936, July 4, cvii, 24.
6. A. MYERSON, J. LOMAN, AND W. DAMESHEK: Physiologic Effects of Benzedrine and its Relationship to Other Drugs Affecting the Autonomic Nervous System. *Amer. Jour. Med. Sci.*, 1936, Oct., cxcii, 560.
7. A. MYERSON: Effect of Benzedrine Sulfate on Mood and Fatigue in Normal and in Neurotic Persons. *Arch. of Neurol. & Psych.*, 1936, Oct., xxxvi, 816.
8. E. DAVIDOFF: A Clinical Study of the Effect of Benzedrine Therapy on Self-absorbed Patients. *Psychiat. Quart.*, 1936, x, 652.
9. W. SARGANT AND J. M. BLACKBURN: The Effect of Benzedrine on Intelligence Scores. *Lancet*, 1936, Dec. 12, 1385.
10. M. RITVO: Drugs as an Aid in Roentgen Examination of the Gastro-intestinal Tract. *Amer. Jour. Roent.*, 1936, xxxvi, 868.
11. M. J. SHAPIRO: Benzedrine in the Treatment of Narcolepsy. *Minnesota Med.*, 1937, Jan., xx, 28.
12. H. M. KORNS AND W. L. RANDALL: Orthostatic Hypotension treated with Benzedrine. *Amer. Heart Jour.*, 1937, xiii, 114.
13. D. L. WILBUR, A. R. MACLEAN, AND E. V. ALLEN: Clinical Observations on the Effect of Benzedrine Sulphate. *Proc. Staff Meet. Mayo Clinic*, 1937, xii, 97.
14. M. H. NATHANSON: The Central Action of Beta-aminopropylbenzene (Benzedrine): Clinical Observations. *J.A.M.A.*, 1937, Feb. 13, cviii, 528.
15. P. SOLOMON, R. S. MITCHELL, AND M. PRINZMETAL: The Use of Benzedrine Sulfate in Post-encephalitic Parkinson's Disease. *J.A.M.A.*, 1937, May 22, cviii, 1765.
16. P. L. DAVIS AND M. SHUMWAY-DAVIS: Orthostatic Hypotension. *J.A.M.A.*, 1937, cviii, 1247.
17. E. GUTTMANN AND W. SARGANT: Observations on Benzedrine. *Brit. Med. Jour.*, 1937, May 15, 1013.
18. E. DAVIDOFF AND E. C. REIFENSTEIN: The Stimulating Action of Benzedrine Sulfate. *J.A.M.A.*, 1937, May 22, cviii, 1770.
19. W. E. EHRLICH AND E. B. KRUMBHAAR: The Effects of Large Doses of Benzedrine Sulphate on the Albino Rat.: Functional and Tissue Changes. *Ann. Int. Med.*, 1937, x, 1874.